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ABSTRACT

This World Health Organization (WHO) report on the proceedings of a Working Group on Child Cancer Control was prepared by the WHO Regional Office for Europe. The working group met in Prague in April 1977 and was comprised of representatives from 14 European countries. Its task was to review existing methods of child cancer control, the efficacy of treatment and management methods, and the possible role of environmental factors. The report presents numerous tables of child cancer morbidity and mortality figures in the European region, and evaluates the positive and negative consequences of treatment of different kinds of malignant diseases and after effects of treatment. Prevention is considered from different points of view: genetic, physical, chemical, and biological. Identification of high-risk groups, effects of environmental factors, and early screening and diagnosis are briefly discussed. Special child-oriented organization of cancer control, including registraction, nomenclature classification and relationship of child cancer control to other health services, is discussed at length. Recommendations are made pertaining to future directions for research in cancer treatment, registration, nomenclature and classification, location of paediatric cancer units, evaluation of delayed side effects of treatment, rehabilitation measures and prevention and early diagnosis. (CM)

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Child Cancer Control

Report on a Working Group

Prague
25–28 April 1977

PS 010213

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World Health Organization
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Note

This report has been prepared by the Regional Office for Europe of the World Health Organization for governments of Member States in the Region and for those who participated in the Working Group on Child Cancer Control. A limited number of copies are available to persons officially or professionally concerned in this field of study from the WHO Regional Office for Europe, Scherfigsvej 8, 2100 Copenhagen Ø, Denmark.

The views expressed are those of the participants in the Working Group and do not necessarily represent the decisions or the stated policy of the World Health Organization

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This report is also issued in French and Russian.

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1. INTRODUCTION

Within the framework of its programmes in maternal and child health (MCH) and cancer, the WHO Regional Office for Europe, in collaboration with the Government of Czechoslovakia, convened a Working Group on Child Cancer Control in Prague from 25 to 28 April 1977. The meeting was attended by 19 temporary advisers from 14 European countries (Austria, Bulgaria, Czechoslovakia, France, Federal Republic of Germany, German Democratic Republic, Hungary, Italy, Netherlands, Poland, Portugal, Sweden, USSR and the United Kingdom). Three staff members of the WHO Regional Office for Europe also attended the meeting. (The list of participants is given in Annex III.) Dr O. Hrodek was elected Chairman and Dr P.A. Voûte acted as Rapporteur.

Welcoming the participants, Dr V. Kusak, Vice-Minister of Health of the Czech Socialist Republic, referred to his Government's interest in paediatric oncology and spoke of the important work being done in Czechoslovakia in that field. Dr D.K. Sokolov, Chief, Strengthening of Health Services, WHO Regional Office for Europe, opened the meeting on behalf of the Regional Director, Dr Leo A. Kaprio. He stressed that it was important, especially in child oncology, to elucidate the etiology and mechanism of carcinogenesis so as to improve methods of prophylaxis, early diagnosis and treatment and the rehabilitation of cancer patients, and to strengthen oncological services. In another address to the opening session of the meeting, Dr P.S. Rönisch, WHO Regional Officer for Maternal and Child Health, spoke of the great need for international cooperation in child cancer control, stressing that child cancer was one of the most important causes of death in childhood. He outlined WHO's policy and recent activities in the field of cancer, emphasizing that the meeting was also to be seen as a follow-up to a consultation meeting at WHO headquarters, Geneva, in December 1972 (*1*).

In the WHO European Region, cancer is one of the major causes of illness and death in children. It is important, therefore, to seek a better understanding of the present needs and demands for services for children suffering from malignant diseases such as leukaemias and solid tumours.

The Working Group's task was to review existing methods of child cancer control, the efficacy of treatment and management methods, and the possible role of environmental factors. An evaluation of the positive and negative consequences of present and future treatment of the different kinds of malignant diseases was also to be made. The special child-orientated organization of cancer control, including registration, nomenclature classification and relationship of child cancer control to other health services, was among the topics to be discussed. Attention was to be given to the physical, mental and social rehabilitation of patients and their families. Prevention was to be considered from different points of view: genetic, physical, chemical

(pharmaceutics and narcotics) and biological. The structure of services (centralization, international collaboration) and the education of physicians and the general public were also to be reviewed.

The Working Group took into consideration the results and recommendations of the WHO Expert Committee on Cancer Control, 1962 (*2*), a WHO Group Consultation on Paediatric Oncology, 1972 (*1*), and the Working Group on the Organization of Comprehensive Cancer Control Programmes, 1972 (*3*).

2. CHILD CANCER MORBIDITY AND MORTALITY FIGURES IN THE EUROPEAN REGION

The morbidity figures for children with cancer, solid tumours and leukaemias in the European Region are not known exactly owing to the inadequacy of registration systems, and it is very necessary to achieve better registration of these figures. According to figures given by various authors, 100–145 children between the ages of 0–15 years per 1 million children will have some kind of tumour (*4, 5, 6, 7*). Leukaemia is the most frequent, followed by tumours of the central nervous system, lymphomas, tumours of the sympathetic nervous system, soft-tissue sarcomas, kidney tumours, bone tumours, retinoblastomas and miscellaneous tumours.

Mortality figures are better known than morbidity figures, and for both girls and boys cancer has been shown to be the second cause of death in all ages. The death rates for different countries do not vary substantially; they show that since 1960 there has apparently been a better prognosis because the death rate has declined. There was a considerable decline in the death rate between 1960 and 1965; from 1965 to 1973 there has been a slower decline. One thing is certain: the number of cases of malignant tumours in children is no greater than before.

The following tables give the death rates from neoplasms among persons of various age-groups in countries of the European Region.

Death rates from malignant neoplasms (A45–A60) by age-groups, per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

Country	Age-groups (years)				
	All ages	<1	1–4	5–14	15–24
Austria	258.7	4.1	7.5	6.3	8.7
Belgium	246.8	8.9	7.9	5.7	8.4
Bulgaria	139.6	1.4	9.0	6.3	10.5
Czechoslovakia	225.7	7.4	9.0	6.8	9.2
Denmark	232.5	8.4	8.2	5.6	8.0
Finland	172.2	1.8	10.0	6.2	7.0
France	215.5	5.9	6.8	5.3	7.3
Germany, Fed. Rep. of	236.6	6.5	7.3	5.9	7.7
Greece	151.1	5.6	9.1	7.0	7.3
Hungary	239.6	7.6	11.2	7.6	9.3
Iceland	145.4	–	5.9	2.2	12.1
Ireland	191.3	4.5	9.0	5.3	10.3
Italy	190.9	4.6	9.3	7.4	8.4
Luxembourg	229.4	–	5.9	1.9	1.8
Malta	113.4	18.6	5.1	13.6	11.0
Netherlands	203.2	9.1	7.1	5.7	6.9
Norway	186.9	9.8	11.1	5.9	7.0
Poland	147.4	6.2	9.5	7.2	8.2
Portugal	135.2	11.8	12.1	7.4	9.1
Romania	124.2	8.0	11.0	7.0	9.7
Spain	143.3	9.8	9.0	6.2	8.1
Sweden	235.2	13.7	5.7	7.0	6.4
Switzerland	208.8	8.0	8.5	6.4	9.2
United Kingdom					
England & Wales	244.2	5.0	7.4	5.6	8.1
Northern Ireland	189.0	13.7	9.2	4.9	7.7
Scotland	248.1	6.7	6.8	3.8	7.0
Yugoslavia	104.7	7.5	7.3	5.2	6.6

– nil or magnitude negligible

Source: **World Health Organization.** *World Health Statistics Annual 1973–1976,* Vol. 1, 1976

Death rates from malignant neoplasms (A45–A60), age-group 0–14, per 100 000 population, in the European Region in 1960, 1965, 1970 and 1973/74 or in the last year for which figures are available

Country	1960	1965	1970	1973/74
Austria	7.0	8.2	7.2	6.5
Belgium	8.1	7.0	7.2	6.4
Bulgaria	7.8[b]	7.7	7.8	6.7
Czechoslovakia	7.3	7.7	7.1	7.4
Denmark	8.0	9.6	7.0	6.4
Finland	7.9	8.2	9.7	6.9
France	7.3	6.6	6.4	5.8
Germany, Fed. Rep. of	7.4	8.1	6.8	6.3
Greece	9.0	9.2	8.0	7.5
Hungary	6.4	7.2	6.8	8.6
Iceland	13.1[a]	4.5[c]	9.1[d]	3.0
Ireland	8.6	6.9[c]	5.5	6.2
Italy	8.3	8.6	7.9	7.7
Luxembourg	1.5	4.0[c]	6.6	2.7
Malta	2.5[a]	2.8	5.6	11.9
Netherlands	8.3	7.6	6.1	6.2
Norway	9.8	8.9	8.7	7.6
Poland	5.4	7.2	7.6	7.7
Portugal	6.6	7.4	7.2	8.9
Romania	7.9[b]	7.3	8.0	8.3
Spain	...	6.6	7.6	7.2
Sweden	8.6	6.9	6.0	7.1
Switzerland	7.8	7.5	6.7	7.0
United Kingdom				
England & Wales	7.8	7.8	6.6	6.0
Northern Ireland	8.6	4.9	6.0	6.6
Scotland	6.8	6.9	6.5	4.7
Yugoslavia	5.2	5.8	6.2	5.9

... not available

[a] B18

[b] 1961

[c] 1966

[d] 1971

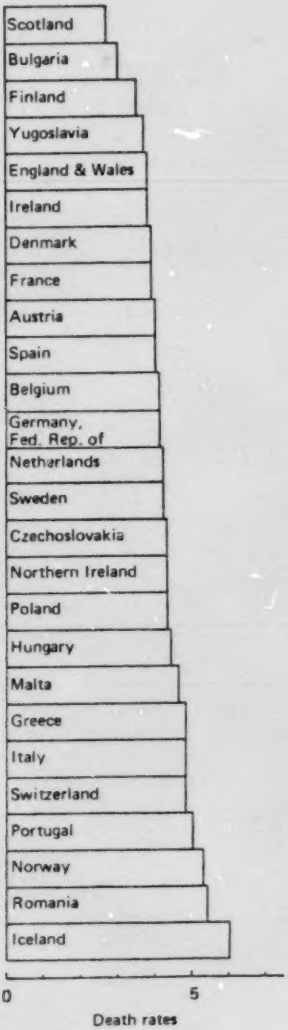
Source: **World Health Organization.** *World Health Statistics Annual 1973–1976,* Vol. 1 1976

Death rates from malignant neoplasms (A59+A60) per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

Females, age-group 0–14 years

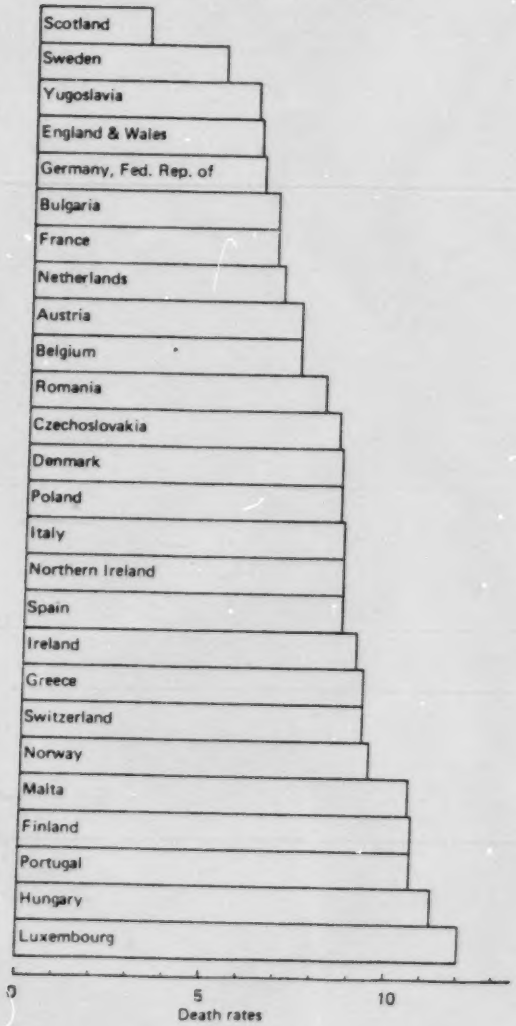
Death rates from malignant neoplasms (A59+A60) per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

Males, age-group 0–14 years



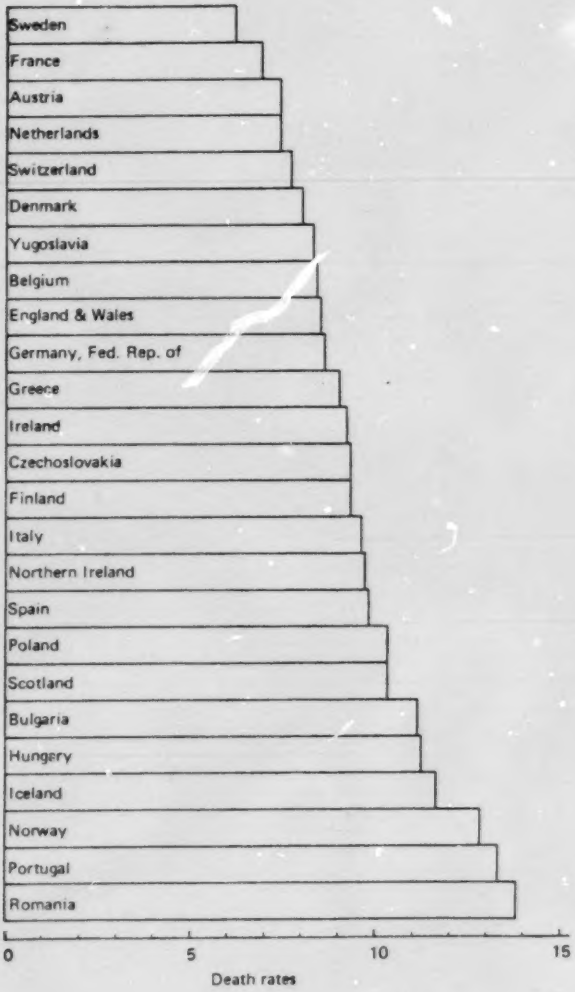
Death rates from malignant neoplasms (A45–A60) per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

Females, age-group 1–4 years



Death rates from malignant neoplasms (A45–A60) per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

Males, age-group 1–4 years

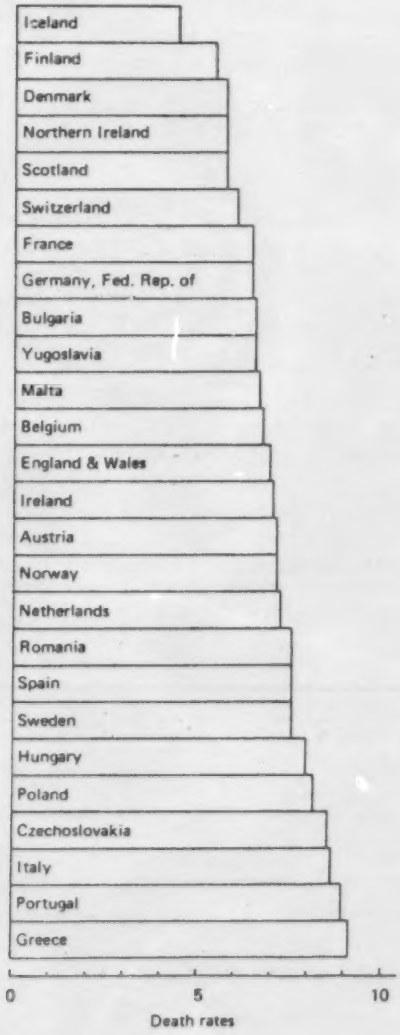


Death rates from malignant neoplasms (A45–A60) per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

Females, age-group 5–14 years

Death rates from malignant neoplasms (A45–A60) per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

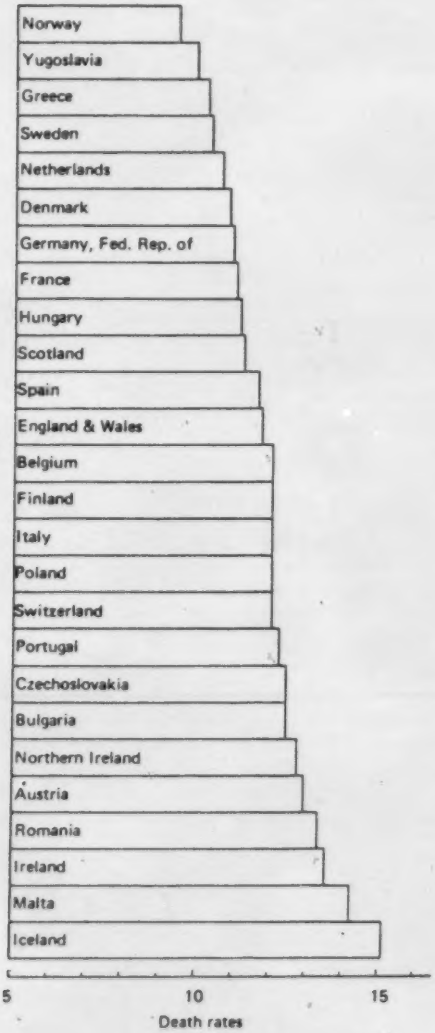
Males, age-group 5–14 years



10

Death rates from malignant neoplasms (A45–A60) per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

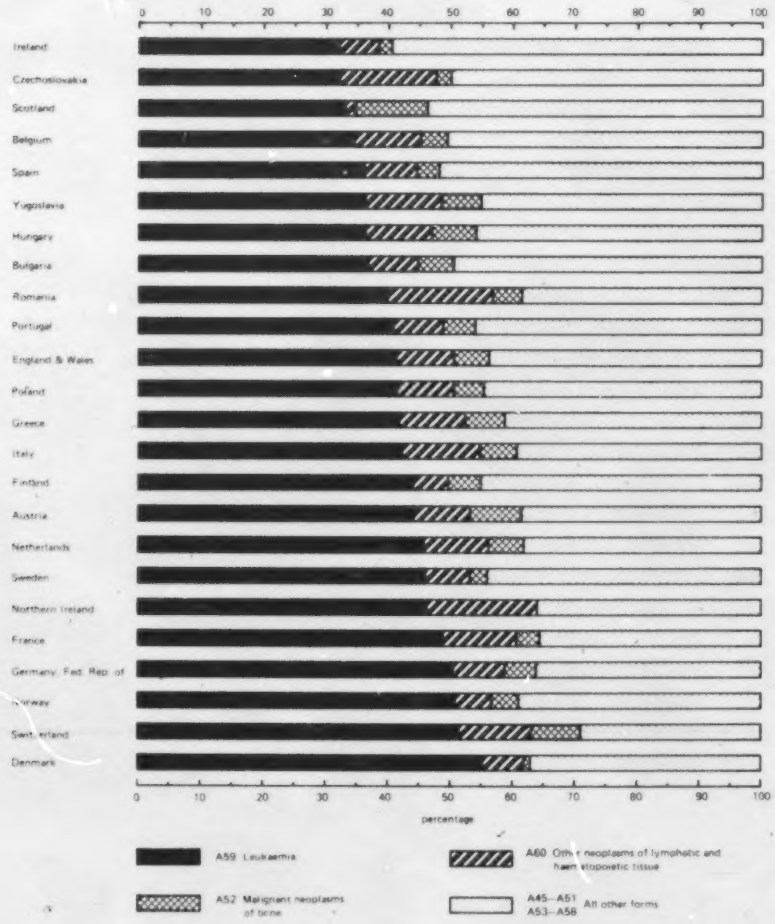
Females, age-group 15–24 years



Death rates from malignant neoplasms (A45–A60) per 100 000 population, in the European Region in 1973/74 or in the last year for which figures are available

Males, age-group 15–24 years

Proportions of different categories of death from malignant neoplasms (A45–A60) in relation to total for the age-group 0–14, per 100 000 population in the European Region in 1973/74 or in the last year for which figures are available



Source: **World Health Organization.** ***World Health Statistics Annual 1973–1976,*** Vol. 1 1976

3. TREATMENT OF MALIGNANT TUMOURS IN CHILDREN

Today, medical science is able to extend the lives of children with malignant tumours and to reduce the severity of their diseases. This is possible not only because the subjects have been treated promptly, but also because tumours in children differ from those in adults. Children have a different biological behaviour and, moreover, are often in a better general condition than adults, both biologically and psychologically, to withstand the treatment. Paediatric oncology is now the subject of considerable interest. Many preliminary reports on treatment are being published, but too often they are based on insufficient material and cover too short an observation period. Nevertheless, it is certain that many patients are being cured and that rates of cure are much higher than formerly. Enormous strides have been made in our ability to care for children with cancer, particularly during the past decade.

Many changes have taken place since the introduction of the first chemotherapeutic agents in 1938, thus marking the beginning of the modern era of cancer chemotherapy. Just as drug treatment involves a combination of agents for most cancers, proper care of the child with cancer also calls for a well-coordinated combination of methods. Effective treatment involves experienced surgeons, paediatric radiotherapists and paediatric oncologists. Optimal care can therefore be provided in a setting where all the necessary components of treatment and support are available.

At the present time, there is little hope of making much progress in reducing mortality from child cancer by means of preventive programmes. Our greatest efforts must be directed towards treatment programmes for children with cancer, especially since there is an increased understanding of the biology of cancer. This has led to improvements in treatment regimens. The treatment regimen still has an advantage in those solid tumours where a surgical approach is indicated. Also, there is a therapeutic advantage in radiation because this can take the form of local treatment. Chemotherapy is the third method of treatment, it is especially important in leukaemia, but is also equal in importance to the surgical and radiotherapeutical approach in solid tumours. In the field of chemotherapy used primarily as an adjuvant treatment, considerable improvements have been recorded in rates of cure, e.g., for Wilms' tumour a cure rate of up to 80% (*8*) can be achieved, and in acute lymphatic leukaemia a cure rate of 50% (*9*) can be reached.

It is important, however, to understand the criteria for "acceptable results". Most of the older literature reported results in terms of one, two, five or ten years of survival. Today, survival alone is an inadequate criteria. A physician is interested in the proportion of patients achieving and maintaining long-term disease-free survival, but with this goal in mind, it is also important to consider the problem of late consequences of the tumour and its treatment.

The impact of cancer and its treatment on growth, development, psychological adjustment, endocrine functions, fertility and the possibility of second malignancies places special burdens on paediatric oncologists. In Europe, where the diversity of languages and of historical and social backgrounds has sometimes presented obstacles in the past, it is necessary to perform collaborative studies on both the registration and the treatment of child cancer cases. Such studies can be performed as clinical trials which would seek not only better methods of treatment so as to improve the rate of cure, but also new treatment procedures that cause fewer side effects.

Joint randomized studies carried out by larger centres are necessary to define the treatment, to ascertain how many patients need radiation and, if they do need radiation, how much is required and how, possibly, reduced fields per dose can be chosen. Perhaps the duration of chemotherapy can be shortened; it may even be possible to end mutilating surgical procedures for certain tumours. The aim for the future should be to establish individualized treatment for each patient. It is an encouraging sign that at the present time this possibility can be considered. This situation has come about because the rate of cure for many tumours has improved and the prognosis for child cancer is far from hopeless (*10*).

4. LATE EFFECTS OF TREATMENT

It is one of the most hopeful situations in the treatment of the child with cancer that we are able to consider the late effects of treatment. Ten years ago the only important thing was how to cure the child. Now, when many patients are cured, interest is turning to the after-effects of treatment. These can be both physical and mental. The former may be caused by surgical, radiotherapeutical and chemotherapeutical procedures, but they may also be late effects on the organic systems, e.g., lungs, intestines, urogenital tract, and on the extremities.

Efforts must be made to avoid surgical procedures which leave serious physical scars, although at present amputations for osteosarcomas, for example, cannot be avoided. However, surgical procedures for urogenital tumours can probably be made less aggressive if the subjects have received chemotherapy. Late effects of radiotherapy are very clear, especially in children (*11*). A child has the full potency to grow, and when one stops the growth potency of part of the skeleton this will have serious implications for the child's future. It is necessary to devise studies aimed at finding ways to avoid these serious complications. Chemotherapy has already resulted in some important complications, such as impaired fertility in adult life (*12*). This aspect would seem to be of special importance when chemotherapy has been administered to children in puberty but not before puberty. A second very important late

effect are secondary malignancies (*13*). Radiotherapeutic procedures bring with them the problem of secondary bone tumours and soft tissue tumours in adolescence and adult life. Furthermore, some chemotherapeutic agents may have the property to cause secondary malignancies (*14*). A well-documented registration system is needed, therefore, so that future patients will have the benefit of accumulated knowledge regarding patients treated earlier.

The psychological late effects of treatment concern not only the patient, but also his family and those around him. The general public has not yet fully accepted the fact that patients with cancer can be cured; thus, the cured patient will be in a very special position. Cured patients must be regarded as being able to lead a socially normal life. In addition, the community has a responsibility to provide jobs for those who have been cured and perhaps also for disabled patients.

Persons cured of cancer should not be subjected to restrictions with regard to their professional occupations. As far as subsequent marriage is concerned, the former patient and his partner should be given full information about the nature of cancer; they should be advised to receive genetic counselling before marriage. Persons cured of cancer may marry and have children, but the children born of such marriages should be closely monitored.

It is an important task of the treatment centre to monitor patients carefully throughout their lives. This follow-up of former cancer patients includes not only the care and treatment of physical side effects, but also attention to their social and psychological well-being. The treatment centre should also be responsible for the care of children of former cancer patients. In this way useful information can be obtained and better ways of treatment developed.

5. PREVENTION

5.1 High-risk groups

It is possible to distinguish several high-risk groups of children who are prone to develop cancer. Most of these patients have one or more congenital anomalies, and this raises the question of the etiology of childhood cancers which seem to have been mostly initiated before birth. Of these congenital anomalies, the following are of special importance:

(a) *Immunological factors.* Congenital immuno-deficiency disorders are known to predispose to lympho-proliferative neoplasias. One example of these is ataxia-telangiectasia, among cases of which a large number of cases of acute leukaemia have been found.

(b) *Hormonal factors.* The dramatic discovery that stilboestrol given to women during pregnancy produced adenocarcinoma or precancerous hypertrophy of the vagina in their daughters was the first demonstration of a transplacental human carcinogen (*15*). In male children, however, there are very few reports of malignancies, although genital abnormalities are found.

(c) *Chromosomal factors.* Chromosomal aneuploidy or fragility are particularly related to leukaemia. The best-known chromosome-linked neoplasm is that associated with Trisome 21 (Down's syndrome) and acute leukaemia (*16*). The second known association of neoplasm with chromosome abnormality is the association of chronic myeloid leukaemia with the translocation of the long arm of chromosome 22 to chromosome 9 (*17*).

(d) *Post-radiation changes.* There have been reports of a correlation between low-level obstetric radiation and cancer and leukaemia in children (*18*), especially in that group of children who also developed an allergic syndrome. The development of developing secondary tumours in children after radiotherapy has also been reported. Children who have received radiotherapy in the neck region are prone to develop thyroid cancer.

(e) *Congenital defects.* There are associations between certain childhood tumours and congenital malformations. The best known is Wilms' tumour associated with growth disorders. These occur in the urogenital tract, in the eye as aniridia and in the limbs as hemi-hypertrophy. They are also associated with patients who have adrenal carcinomas or hepatoblastomas (*19*). It is important that these facts should be known to obstetricians, general practitioners and ophthalmologists so that when such abnormalities are noted in infancy, the children can be closely monitored.

(f) *Double primary tumours.* It is known that patients successfully treated in infancy for a retinoblastoma, may develop a second primary tumour, often an osteosarcoma. This tumour may occur locally as a result of radiotherapy, or become widespread without previous irradiation (*20*).

One of the objectives of general registration of children with cancer in Europe will be to arrive at a better understanding of which patients belong to the high-risk groups. Moreover, establishing these high-risk groups can provide the key to the etiology of these tumours.

5.2 Environmental factors

Not much is known about environmental factors, but viral infections, for instance, are among these: in Africa, Burkitt's lymphoma and its association with Epstein-Barr virus infection is, although not definitely established, quite convincing. The link between asbestos and cancer is clearer. It has been reported that children in families where men worked in asbestos factories

developed mesothelioma in later life. It is assumed that the dust was brought back in the men's clothing and affected the children.

The health implications of nuclear power production have already been the subject of a report by the WHO Regional Office for Europe (*21*).

5.3 Screening factors

Much study has been carried out on screening factors and on ways of arriving at an early diagnosis in children with cancer. Except for children in the high-risk group, screening factors have not proved useful, generally because most of the tumours are seldom encountered. As stated above, one can expect to find 100–145 patients per million children between 0–15 years. Since one-half of them are leukaemias, all the other tumours will be found even less frequently. Out of one million patients, only five with Wilms' tumour and approximately 10 with neuroblastoma can be expected. Possibly this last group could be subject to screening because the diagnosis can be made on urine findings, but it would be highly impractical to investigate 1 million children to discover 10 patients at an early stage. The same is true for patients with hepatoma or germ cell sarcoma who have an enlarged level of alpha-pheto protein in their serum. These tumours are encountered less rarely than neuroblastomas. So far it has not been possible to employ screening methods, but they are of importance for patients belonging to the high-risk group.

6. ORGANIZATION OF CHILD CANCER CONTROL SERVICES[a]

6.1 Nomenclature and classification

Although childhood tumours are rare diseases, the increased attention being paid to these tumours has raised the problem of describing cases more accurately. This has become necessary for the purpose of registering cases for epidemiological studies, for clinical trials and for comparing the results of therapeutic procedures used in different centres. The description of a cancer case will include the following:

(a) patient identification, with age and sex;

(b) tumour identification: morphology of tumour in microscopic examination;

[a] See Annex I, p. 29

(c) location of tumour: indication of anatomical site of tumour;

(d) extent of tumour: size and extent of primary involvement of regional and juxta-regional lymph nodes and metastatic spread.

Much work on this subject has been done by the International Society of Paediatric Oncology (SIOP), the International Union Against Cancer (UICC) and the American Joint Committee (AJC). It has been carried out in close conjunction with the WHO International Classification of Diseases for Oncology (ICD–O) (*22*).

6.1.1 *Morphology of childhood tumours*

It is recommended that the morphology section of ICD–O be adopted without change.

6.1.2 *Size of tumours in children*

Several anatomical nomenclatures are available, none of which is particularly suitable in relation to tumours in children. The most widely used is the topography section of ICD–O. However, several oncology centres have found that ICD–O was unsuitable for paediatric oncology, mainly because of lack of specificity in some areas or of useful specificity in other areas where tumours are exceptional in children. A special topographical coding may have to be designed for childhood tumours instead of simply subdividing the ICD–O categories. Nevertheless, this coding system should be compatible with ICD–O in the sense that ICD–O categories could be derived automatically from it.

The coding system designed by a group of SIOP members could possibly be used for the topography of tumours in children. This system is based on divisions into main regions, large areas such as head and abdomen, and subregions, further defined areas such as face or retroperitoneum, sites such as the eyeball, and structures such as skin or deep soft tissues. The code has a four-digit number indicating the above-mentioned categories. However, in childhood tumours special cases should be included, such as tumours involving several regions or multiple disseminated tumours. In the European Region stimulus should be given to the production of a workable system for tumour sites in children which can be regarded as complementary to ICD–O, which is used for tumours in adults.

6.1.3 *Extent of tumour*

The extent of tumours in adults is described in the TNM and Staging System. In paediatric oncology, staging is commonly used in a very pragmatic way and prognostic studies have shown that, in the majority of the cases, stage is well correlated with survival. But for many tumours there is more than one

staging system in use, and each major institution or at least each country has its own system. Usually the differences are not important, but they are sufficient to create a great deal of confusion and to make it impossible to compare series of cases staged differently. Besides, the definition of stages is arbitrary, pointlessly different for different tumours, and is based mainly on surgical findings and on therapeutic policy considerations which are subject to change.

SIOP also decided to design a classification for the commonest paediatric tumours such as Wilms' tumour, neuroblastoma and soft-tissue sarcomas. A classification has to be as simple as possible; in addition, an attempt must be made to base it on the TNM categories, although the TNM system has not yet penetrated the world of paediatric oncology. This system has first to give a description, as accurate as possible, derived from clinical and surgical findings.

Staging comes after this description; it is an arbitrary arrangement of the clinical and surgical findings, made mainly for the purpose of defining treatment indications. It is proposed that this paediatric TNM-staging system should be a 2-step-system: (1) clinical and radiological, and (2) surgical and pathological. The TNM system is based on the assessment of:

(a) the extent of the primary tumour – T;

(b) the condition of the regional and juxta-regional lymph nodes –N;

(c) the absence or presence of distant metastases, including lymph node involvement beyond the juxta-regional nodes – M.

Clinical TNM is based on clinical and radiological examinations before any treatment is given. Mandatory examinations are specified for each tumour; if not available "X" can be entered.

The surgical and the pathological system will be called PNM and will be based on evidence derived from surgical operations and histopathology.

It is of the utmost importance that this work should be furthered, since it is the only way to achieve a common clinical language in European paediatric oncology centres. The coding system should be uniform and as simple as possible.

6.2 Treatment centres

6.2.1 *Functions*

The various functions which a centre for paediatric oncology has to fulfil will now be considered.

Patient care

Patient care may be divided into medical technology, nursery care and psychosocial care. All three are equally important in the care of children with cancer. As far as medical care is concerned, the centre must be equipped with the best possibilities for diagnosis and therapy, and must also have the equipment to enable it to carry out follow-up studies of the quality of the care given. Therapy should be completely child-oriented. Under the supervision of a paediatric oncologist, the paediatric surgeons, paediatric radiotherapists, paediatric pathologists and other specialists concerned with child care should work together during the initial treatment. Depending on local situations, e.g., travelling distance of the patient and his parents, follow-up treatment may be given under the supervision of a local doctor, whether a paediatrician or a general practitioner. This follow-up treatment should be in line with the treatment methods planned by the centre.

Concerning nursing care, and specifically the number of nurses needed in connexion with the treatment of children with cancer, it is clear that more nurses are needed in this field. It should be pointed out, however, that the mental burden on nurses caring for children with cancer is great.

With regard to psychosocial care, a centre must be equipped with the means to provide the necessary psychological care for the child and its family. The education of the child during its illness should not be neglected.

Rehabilitation also forms part of this psychosocial care. Even if a treatment centre lacks all the necessary facilities, they should be available at not too great a distance from the centre.

Research

A subdivision may be made in research activities on the basis of the different stages of the acquisition of knowledge.

(a) *Basic research.* The child oncology centre needs to have close contact with a basic research institute where fundamental investigations are being carried out on the nature or etiology of cancer.

(b) *Developing research.* Developing research is orientated towards finding better ways of treating cancer patients. It is primarily pharmacological, but newer techniques in radiotherapy or surgery may also be developed. This has to be done experimentally before the results can be applied to the cancer patient. These research institutes need to maintain close contacts with the treatment centres.

(c) *Applied research.* The possibilities deriving from basis research and developing research can be applied in a clinical situation. One of the topics of this research will be the programmes of clinical control trials which have to be carried out in cooperation with other institutes working in the field of child cancer.

Education[a]

Education is one of the most important aspects of the treatment centre. The education will be medical and will be offered not only to medical students but also to physicians training to become specialists. Postgraduate training with a view to making new knowledge accessible is a necessary task of the centre. The education of all medical personnel should be on a continuing basis; it is one of the most important methods of ensuring an early diagnosis of the patient and thus of securing better treatment results.

The second aspect of education is the training of nurses. Here, too, education needs to be continuous because the nursing personnel are in very close contact with the patient. Instruction in new methods of treatment and the reasons for them will achieve better treatment results.

Thirdly, the education of auxiliary health personnel, such as social workers and psychologists, is important. They too have to know what kinds of treatment are given, what can be expected of the treatment and how patients and their families can best be supported.

A fourth aspect is the education of the general public. They should be instructed about conditions and circumstances in which cancer and tumours may occur, and it should be stressed that an early diagnosis is of great importance in that it increases the possibilities of successful treatment.

If the educational aspects of the treatment are emphasized the result will be an improvement in the functioning of the centre, because a greater degree of motivation on the part of staff, patients and their families will be achieved.

6.2.2 *Population-based centralization*

In most European countries much has been done to establish community cancer care services, yet these organizations are mainly aimed at providing care for adults. In the economically developed countries, mortality from cancer in children has risen to second place and is now attracting close attention on the part of health administrations; the establishment of paediatric cancer care services has thus become a topical question. Of course, it will be essential to obtain actual data on the true frequency of malignant tumours, as stated above. The child cancer registry has to be closely linked with the general cancer registration system of the country or region.

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[a] See Annex II, p. 33

Morbidity figures are not available, although some approximate figures are known, but mortality rates can be obtained from WHO sources. However, figures from individual child cancer registries indicate that there is a morbidity of 100–150 per million of the child population. Fairly accurate figures have been obtained from the USSR. In Leningrad the incidence of malignant cancer morbidity among children aged 0–13 years was 7–11 per 100 000 of the child population in 1958 and 8.2–12.5 in 1964. A more accurate registration begun in 1966 showed an annual cancer morbidity of 15.8 per 100 000 of the child population. Approximately the same figures have been obtained from the Moscow area.

If one takes into account the number of patients likely to be encountered one may conclude that the most suitable ratio would be 1 child oncology centre per population of 4–5 million. A centre set up on this basis would gain sufficient experience in treatment because it would receive a large enough number of patients to do its work properly. It could also give the necessary total care. Centralization of treatment is important because the different tumours are still rare and patients should have the benefit of the experience acquired in a child oncology centre. The number of beds necessary for a unit will depend very much on local and social conditions. These may differ widely in the European Region. There are countries where most mothers are in employment and the social situation thus makes it impossible for the child to convalesce at home. In other situations the costs of hospitalization may be high and care could equally well be given at home after a short period of hospitalization. A total of 40 beds per centre, for both inpatients and outpatients seems necessary. Special financial support is required from governments so that the centres can attain a high standard of medical and psychological care and in order that the necessary research efforts into causes of child cancer can be intensified.

6.2.3 *Location of child oncology centres*

When the organization of child cancer control services is being considered, the location of child oncology centres is of great importance. Such a centre can never exist completely on its own: paediatric oncology will always be a part of paediatrics as a whole, but it is also a part of the specialty of oncology. The two places most suitable for the location of a child oncology centre are a general children's hospital with all the facilities essential for the care of children, or a cancer institute with a special paediatric unit. If the paediatric unit is located in a cancer institute, it must contain all the necessary services for hospitalized children, including psychological, social and educational services.

For medical and economic reasons it is important that there should be close links between the cancer centre, the general hospital and blood transfusion services so as to prevent any duplication of medical activities. In such a framework an adolescent cancer unit could also be set up in conjunction with

a paediatric cancer centre. An adolescent cancer unit may not be possible in all situations. In that case each adolescent patient should be evaluated on an individual basis and placed either in a child unit or in an adult unit on the basis of the adolescent's developmental age rather than his chronological age. In addition, the child oncology centre needs to have links with the peripheral services, which are part of the general health system of the country concerned.

7. RECOMMENDATIONS

Achievements in cancer treatment

(1) The achievements in cancer treatment over the past ten years should be assessed by means of collaborative clinical studies and trials, with statistical analysis, on an international basis.

(2) In the light of achievements leading to a better rate of cure for children with cancer, an international study on the early and late effects of treatment should be conducted.

Registration, nomenclature and classification

(3) A uniform and simple system of staging following the TNM system should be used, and work being carried out by competent bodies in this field should be supported.

(4) The uniform morphological classification system contained in ICD–O should be followed.

(5) The development of a tumour site classification compatible with ICD–O should be encouraged.

Location of the paediatric cancer unit

(6) The paediatric cancer unit should be part either of a cancer institute or of a children's hospital, and there should be close links with a general hospital and a blood transfusion service; the unit should also be linked with a research unit.

(7) The unit should have a paediatric surgical section which is cancer-orientated, and should have among its staff specialist paediatric cancer surgeons, paediatric radiotherapists, paediatric oncologists and pathologists.

(8) The unit should have an environment that is psychologically orientated towards children.

(9) The unit should have a positive approach to comparative studies carried out in collaboration with other institutions in this field.

(10) The primary treatment of patients should be centralized.

(11) Secondary treatment should be provided in cooperation with local health workers.

(12) Adolescent cancer units should be linked with paediatric cancer units.

Evaluation of delayed side effects of treatment

(13) The paediatric cancer unit should maintain continuous monitoring of patients to check for possible delayed side effects, and should study, in co-operation with a paediatric clinic, ways of avoiding these side effects.

Rehabilitation measures

(14) The child cancer patient should be helped to participate in normal school activities in preparation for a suitable future occupation.

(15) Mental, social and physical rehabilitation should be part of the total therapy and should be carried out in conjunction with the patient's family.

(16) If the death of a child cancer patient is considered likely, rehabilitation measures should be extended to the family before and/or after death occurs.

Prevention and early diagnosis

(17) Children with congenital anomalies which are known to be associated with cancer should be carefully monitored.

(18) Hereditary cancers and cancers in families should be registered on the basis of a multidisciplinary approach.

(19) Epidemiological studies on cancer should be conducted simultaneously and along parallel lines in children and adults.

(20) Children cured of cancer should be advised to receive genetic counselling before marriage.

(21) Financial support should be given to paediatric cancer units to enable them to develop methods of prevention and early diagnosis in respect of high-risk groups.

Centralization of services

(22) Paediatric cancer units should be set up on the basis of 1 unit to approximately 4 million child population; there should not be a proliferation of small centres with an insufficient accrual rate and insufficient staff.

(23) The unit should provide both education for medical personnel and public information.

(24) Registration of child cancer should be carried out on a national basis in such a way that the resulting data are internationally comparable, and uniform data systems should be developed and followed.

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Annex I

THE ORGANIZATION OF CHILD CANCER CONTROL SERVICES

Professor L.A. Durnov[a]

Of the many problems in the field of child cancer, one of the most important is the organization of paediatric cancer control services. In many countries much has been done to establish community cancer care services, but these organizations are intended mainly to provide care for adults. This situation has arisen because until the nineteen-fifties paediatric efforts were directed at the control of early infant mortality, infectious diseases and other conditions. In the last 20 years, however, child mortality from cancer in economically developed countries has risen gradually to become the second most important cause of death among children. It is now attracting close attention on the part of health administrators in a number of countries, and the establishment of paediatric cancer care services has become a topical question.

It goes without saying that, in establishing any cancer control programme, it is essential to obtain accurate data on the true frequency of malignant tumours. However, although data on mortality rates from malignant tumours in children can be obtained from WHO sources, there is an almost complete absence of such figures relating to morbidity. There exist only publications from a number of treatment establishments, but these naturally do not reflect the true morbidity. Reporting and evaluation documentation does not always contain graphs showing the breakdown by age-groups (0–1 year, 2–4 years, 5–9 years, 10–14 years) and as a result it cannot be used to form a sufficiently accurate picture of child morbidity from malignant tumours, or of the structure of morbidity, and this in turn hampers the establishment of care services for child cancer. However, data from individual child cancer registers indicate that there is an annual mortality from malignant tumours of 13–16 per 100 000 of the child population.

In the USSR, work on cancer registration among children is being conducted in Moscow and Leningrad. In Leningrad, the incidence of malignant cancer morbidity among children aged 0–14 years was 7–11 per 100 000 of the child population in 1958 and 8.2–12.5 in 1964. More accurate registration, begun in 1966, established an annual morbidity rate of 15.8 per 100 000 of the child population from this cause. Approximately the same figures have been obtained from Moscow and a number of other parts of the country.

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On the basis of selective data, it may be estimated that there is at present an annual world-wide morbidity from malignant cancers of more than 250 000 children. Judging from many reports, it seems that this figure will rise in the coming years, as child cancer morbidity is displaying an upward trend.

Thus, the first task is to establish a child cancer registration service: this may be done by nationwide state registration (the most comprehensive form of registration) where this is possible, or by the establishment of special registration centres which should include hospital cancer registers. If data are to be obtained more swiftly, the establishment of a number of different centres for the registration of child cancer may be contemplated for geographically, economically and socially different areas. Child cancer registration presupposes work on the classification of child cancers. Unfortunately, there has so far been no uniform classification of child cancers and this is hampering the registration of tumours, preventing the comparison of results, and hindering collaboration among workers in the field of paediatric oncology.

If reliable information on child morbidity from malignant tumours can be obtained, it will assist in proper planning for the development of specialized child cancer departments. Provisional studies of this type have been carried out in the USSR. For example, on the basis of data received from child cancer specialists in Leningrad, and taking into account both the morbidity of children from malignant and benign tumours and the time taken to treat patients with different types of tumour, it is essential to plan for 4.2 beds per 100 000 in the 0–14 years age-group, or the establishment of specialized child cancer departments of 50–60 beds. Such departments can meet the needs of an administrative district with a population of 3.5–4 million inhabitants.

The establishment of specialized child cancer departments is imperative since they are essential to the logistics involved in establishing a child cancer care service. It is in specialized departments that the most highly skilled care can be supplied and therefore the treatment results obtained in them are considerably better than those obtained in general child hospitals. There has been considerable progress in the last few years in setting up specialized child cancer departments. While, as a whole, the overall recovery rate for children suffering form nephroblastomas in all children's and cancer hospitals is no greater than 5–10%, there is a recovery rate of more than 50% of such patients in specialized departments, and in many of these clinics the rate of recovery for patients entering at an early stage in the progress of the disease is as high as 90%. Similar data can be obtained in respect of other neoplasms.

Experience shows that because of the small number of specialized child cancer departments, often located at considerable distances from each other, it is essential to appoint paediatric oncologists to major cancer outpatient treatment departments if children suffering from malignant tumours are to be treated swiftly. This type of specialist would be used not only to conduct the initial consultation for children suspected of suffering from a tumour, but also

to ensure properly planned hospitalization and follow-up outpatient observation, and, in addition, to conduct preventive treatment, where this is required or practicable.

Specialized departments and paediatric cancer consultancy posts must be located in such a fashion as to cover as wide a range of children as is possible. In establishing them, convenience of transport and access and a number of other factors must be taken into account.

These factors give rise to staffing questions. At the present time there are insufficient qualified paediatric cancer specialists. This is bound up with the fact that medical personnel are not being trained in this specialty: no such specialty as "child oncology" is being taught. There has only been a small amount of preliminary experience in teaching child oncology at medical schools (Moscow and Leningrad). At the same time, a study of child patient admissions for malignant cancers to inpatient establishments shows that the vast majority of children present at far advanced stages of the diseases (60–75% of all patients), and this situation is aggravated by the fact that diagnostic mistakes have occurred in 55.7% (Leningrad) or 65% (Moscow) of them.

Child inpatient admissions at advanced stages of cancer development are referred to in nearly all reports on child cancers made by workers from many countries and, to judge from them, the percentage of such children is very high (about 70%). It is therefore essential to introduce the teaching of child oncology in paediatric faculties and in faculties providing continuing education for physicians. This leads to the idea that it might be worthwhile to produce a textbook on paediatric oncology which would contain the latest knowledge on the subject, and which could be prepared jointly by specialists from different countries so as to make it more universally applicable and comprehensive.

The paediatric cancer campaign must be closely linked with scientific research in the same area. Unfortunately, scientific research on this subject is being carried out in random fashion: there are no coordinating centres, and international cooperation in the field is poorly organized.

One useful example would be some of the programmes for cancer control adopted by cancer specialists treating the problem in the adult population (for example, in the field of cancer epidemiology). At the same time, even a superficial glance at the epidemiology of cancer among children gives rise to the following questions:

(1) Why is it that in France 57% of all those children suffering from malignant cancer die of acute leucosis, while the equivalent figure in Sri Lanka is only 30%?

(2) Why is it that 17.3% of child patients in Israel die of reticulosarcoma, while in Poland only 3.4% of all children with malignant tumours die from the same condition?

(3) Why is it that 6.5% of children suffering from tumours of the central and peripheral nervous system in Japan die, while the figure for Australia is 28%?

(4) Why, in New Zealand, do cancers of the gastrointestinal tract make up 0.5% of all child cancer mortality, while in Sri Lanka they account for 13.7%?

Scientific research work could be conducted by child cancer centres already established or to be established in different countries and areas. As with adult cancer, scientific research into child cancer is best conducted where children with malignant tumours are treated. There are a number of examples that may be cited in support of this, including the USSR Academy of Science's Cancer Research Centre. This centre possesses a department which includes children's clinics with 100 beds, and a scientific paediatric polyclinic department. This institution is, at the same time, the cancer registry for Moscow, and is being used as a base for training qualified paediatric cancer specialists, where scientific and practical work are carried out together.

Annex II

EDUCATION IN PAEDIATRIC ONCOLOGY

Dr O. Hrodek[a] and Dr J. Koutecký[b]

Education in paediatric oncology is an extremely important part of the general campaign to control malignancies. The success of any cancer control programme will to a large degree depend on it. New facts discovered in the study of malignant tumours as well as advances in their treatment with a view to long-term survival or even in some cases cure make it imperative to work out a well organized system of education at all levels.

Like other specializations concerned with the physiology and pathophysiology of childhood, paediatric oncology differs from adult clinical oncology in a number of special ways, which all educational efforts must take into account. The ever expanding scope of these differences must be the concern of all persons who come into contact with children in any way, and with children suffering from tumours in particular. Such persons include:

(1) the general public (parents and relatives looking after children, school workers, nursery personnel, sports organizers, etc.),

(2) auxiliary health personnel,

(3) paramedical personnel (paediatric nurses, laboratory and rehabilitation workers, social workers and psychologists),

(4) medical students (undergraduates),

(5) general practitioners,

(6) paediatricians,

(7) paediatric specialists (paediatric surgeons, neurologists, gynaecologists, otolaryngologists, roentgenologists, etc.),

(8) general clinical oncologists,

(9) paediatric oncologists.

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The general public

Members of the general public, particularly if they are in any kind of contact with children, should in principle be kept informed, in a suitable way and to an adequate degree, about some of the principal features of cancerous diseases in childhood. Briefly, this involves information on :

(1) the possible incidence of all sorts of tumours in any period of childhood;

(2) the rate of incidence of tumours in children;

(3) their symptomatology, however vague;

(4) the significance of early detection for therapeutic results;

(5) the significance of observing changes in the child;

(6) present-day therapeutic opportunities;

(7) the general results of treatment;

(8) the damage caused to subsequent diagnostic and therapeutic procedures by unsubstantiated fear, pessimism, and misleading nihilism;

(9) the principles of psychology with regard to tumour-affected children and their families;

(10) the right to prompt special medical investigation and treatment at specialized paediatric oncological institutions;

(11) basic preventive measures, i.e., elimination of harmful habits, correct diet, food storage and preservation, abstinence from smoking, personal and environmental hygiene, and on the need for preventive check-ups.

Auxiliary health personnel

These persons, particularly when they are in contact with children with tumours, should be kept informed about all the above points (1–11) in more detail and, in addition, about:

(1) the basic biology of neoplastic disease, particularly as regards the treatment of children (e.g., handling them in general, under anaesthesia, during fixation on the examination or operation table, during transportation, etc.), and about the hazards of dissemination in case of tumour injury due to mishandling;

(2) informing the relatives about the child's condition;

(3) the need for caution in conversations in front of the patients.

Paramedical personnel

These persons must be adequately knowledgeable about all the points listed above in line with their specialized role in the oncological programme. Those working in special departments of paediatric oncology must also be adequately versed in:

(1) the principles of basic methods of investigation in paediatric oncology (their essence, methodology and technique);

(2) the principles of all therapeutic procedures (their essence and methodology, contraindications, complications, their symptomatology and treatment);

(3) psychological problems of sick children and their families;

(4) the psychology of their own approach to cancer and to all the circumstantial facts involved in work with tumour patients;

(5) social problems affecting patients with cancer.

In educating this category of workers, points 2–4 are of more concern to nurses working in wards, whereas the education of laboratory workers should be specially extensive with regard to point 1, in accordance with their specialization (haematology, roentgenology, biochemistry, histology, cytology, etc.). Rehabilitative, social/educational and psychological workers should have a particularly good command of the points concerning the psychological and social problems involved in paediatric oncology.

Medical students

These persons must acquire a good command of all the above points to the required extent and on a scientific basis, so as to have a full grasp of all the biological, diagnostic and therapeutic problems of cancer in children, and to avoid any erroneous procedures in their future practice. They should be brought to understand the existence of paediatric oncology and its exclusive position in the case of tumour-affected children, and to take the *lege artis* approach whenever there is the slightest suspicion of cancer. In addition to all the above points, a medical student is expected to gain command of:

(1) the principles of the pathological anatomy and histology of specific childhood tumours;

(2) the principles of the pathological physiology of tumours;

(3) the principles of special paediatric oncology;

(4) the principles of prevention in paediatric oncology (in connexion with the knowledge of present-day ideas on the etiology of malignant growth).

Paediatric oncology should be taught by specialized paediatric oncologists within the framework of a coordinated and integrated undergraduate teaching programme. As in other branches of medicine, it is hardly possible to include new knowledge in the programme by claiming more teaching hours or cramming the curriculum. Here, too, the general principle applies, namely that of rationalizing the teaching effort by linking together, horizontally and vertically, all the clinical specializations, malignancies being included under the systems affected.

General practitioners

The postgraduate education of general practitioners ought to include regular information on new developments in paediatric oncology, studies of mistakes, results and prospective plans. The two components of education and specialization should be suitably combined. This line of education should be controlled from the centre in keeping with present and future needs of the health care system within a given framework of health services and postgraduate medical education.

Paediatricians

The same, though at an appropriately higher level, applies to these persons, whether they work in the field or in general departments of paediatrics. Education in paediatric oncology should be included in their postgraduate specialization courses. The aim of this line of education in paediatric oncology is to achieve a maximum reduction in the time factor, i.e., the period between recognizing the first subjective or objective signs of disease and admission to a specialized department.

Their education should be centrally controlled so as to bring their standard up to a good average and to give an equal chance to each child. Instruction should be continuous and provided by a specialist in paediatric oncology. Information given to the patient's relatives should be without too much detail so as to avoid giving the wrong ideas to parents and affecting their mental condition more than is necessary. Moreover, these doctors are expected to acquire a basic knowledge of:

(1) the perfect methodology for clinical investigation in oncology;

(2) completion of the treatment of the underlying disease (according to the specialists' recommendations), its complications, any therapeutical complications, etc.;

(3) methods of work with outpatients;

(4) expert views concerning the child's inclusion in a children's team, the use or exclusion of any activity (e.g., sports), recommendations concerning the child's working capacity.

Paediatric specialists

Such specialists must have a perfect knowledge of special oncological matters (principles of diagnosis and treatment of tumours affecting the different organs or systems, including specialized surgery), and be educated in the principles of comprehensive oncological care controlled by a paediatric oncologist. They should be trained to participate in the process of making decisions on the plan of treatment, as well as on the plan of after-care.

General clinical oncologists

These should be made acquainted with the specific problems of paediatric oncology so as to be certain, within the framework of their specialization, about the differences in the problems of tumours in childhood as opposed to adult oncology and to accept paediatric oncology as an independent specialization in keeping with objective facts. Continuous postgraduate training on advances in paediatric oncology should be given them at regular intervals.

Paediatric oncologists

The education of these persons should be controlled by a central institution and brought up to the highest possible level with a view to establishing central institutes of paediatric oncology. The training should include:

(1) the specialists' own studies of the recommended literature, and an acquisition of knowledge at existing institutes of paediatric oncology;

(2) specialized education in centrally controlled short-term courses or at teaching institutions of paediatric oncology;

(3) education by highly specialized experts (through international co-operation) with a view to their practice and research in special fields of paediatric oncology, including participation in international working groups concerned with the treatment of different tumours in children.

Annex III

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